



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/887,496	06/22/2001	Partha S. Banerjee	1121.0206-US1	7707
20311 7590 07/22/2009 LUCAS & MERCANTI, LLP 475 PARK AVENUE SOUTH 15TH FLOOR NEW YORK, NY 10016				
EXAMINER KANTAMNENI, SHOUBHA				
ART UNIT		PAPER NUMBER		
1617				
NOTIFICATION DATE		DELIVERY MODE		
07/22/2009		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

info@lmiplaw.com

Office Action Summary

Application No.

09/887,496

Applicant(s)

BANERJEE ET AL.

Examiner

Shobha Kantamneni

Art Unit

1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 March 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 3-21, 23-38, 40-64, 69-74, 78-83, 87-89, 93 and 99-146 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) NONE is/are allowed.
- 6) ☒ Claim(s) 1, 3-21, 23-38, 40-64, 69-74, 78-83, 87-89, 93 and 99-146 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

This office action is in response to applicant's response filed on 03/30/2009.

The rejection of claims 1, 3-21, 23-38, 40-64, 69-74, 78-83, 87-89, 93, 99-128, 129-146 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of US Application No. 11/688436 (US Patent No. 7,465,756), over claims 1-18 of U.S. Patent No. 7,348,362, over claims 1-88 of U.S. Patent No. 6,667,344, and over claims 1-73 of U.S. Patent No. 6,814,953 in view of Carling et al., PDR is herein withdrawn. Note that applicant has filed Terminal Disclaimers.

Claims 1, 3-21, 23-38, 40-64, 69-74, 78-83, 87-89, 93 and 99-146 are pending, and examined herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3-21, 23-38, 40-64, 69-74, 78-83, 87-89, 99-112, 117-119, and 122-128 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hochrainner et al. (US 6,150,418, PTO-892 of record) in view of Carling et al. (US 5,674,860, PTO-892 of record), and PDR.

Hochrainer et al. discloses propellant-free pharmaceutical composition comprising formoterol or its salt, or addition products (preferably, formeterol fumarate as salt, hydrate as addition product), a known bronchodilator, particularly stable on storage with concentration 10 –500 mg/ml (see col.1, lines 37-46, lines 65-67; col.2 lines 6-11), in aqueous ethanol, and ethanol mixture (water and ethanol are well known polar and protic solvents, see col.2 lines 24-34), in the form of a solution or suspension for use in inhalers for nasal therapy, see abstract and claims 1-4, 8 in particular. Hochrainer et al. further teaches that the pharmaceutical composition is such that it can be administered by inhalation using a suitable nebuliser, see col.4, lines 19-20 and col. 5, lines 33-41. Hochrainer et al. teaches that the pH range is preferably between 2.0-7.0 and most preferably between 4.5-5.5. The employment of inorganic acids, and organic acids such as phosphoric acids, citric acid, tartaric acid, fumaric acid etc. and the employment of buffers in its composition are also taught, see in particular col.3, lines 35-40 and col.4 line 55 to col. 5, line 7; and inorganic salts, sodium chloride, and organic salts such as for example, sodium, potassium or ammonium salts of citric acid, Na-EDTA (see col.2 lines 56-64, col. 4, lines 55-57) in the composition is also taught. Hochrainer et al. teaches the concentration of formoterol to be between about 75 mg/ml and about 500 mg/ml, which may be used with diluent, and other ingredients for the preparation of therapeutical composition. See in particular claims 1-4. Hochrainer et al. also teaches that additional active ingredients such as steroids, anticholinergics could be incorporated in its composition, see claim 19. It is taught that the pharmaceutical preparation suitable for administration is obtained by diluting the active substance

concentrate with a pharmacologically suitable solvent. See column 4, lines 21-25. It is taught that the formulation for administration is obtained by diluting to 0.9 mg/ml of formoterol with the diluents such as water, aqueous saline and the PH is adjusted for stable storage. See column 4, lines 26-29; column 5, lines 1-6. A formulation containing a solvent mixture of ethanol/water, formoterol in a concentration of about 0.9 to about 1.5 mg/ml adjusted to a pH of about 4.5 to about 5.5 is also disclosed. See column 8, claim 22. The pharmaceutical compositions therein can contain surfactants for stabilizing suspensions or other stabilizers which include sorbitan esters which reads on instant Polysorbate 80. See column 3, lines 10-27.

Hochrainer et al. also discloses a kit or an article of manufacture comprising the same combination and packaging material include containers, nebulizers. Preferred nebulizers include inhalers. See column 5, lines 33-47. The compositions therein are employed in the methods of treating obstructive respiratory diseases and asthma, see col. 1, lines 1- 37.

Hochrainer et al. does not teach particularly the employment of a steroidal anti-inflammatory agent, fluticasone propionate, and its concentration.

Hochrainer et al. does not explicitly teach the concentration of formoterol such as 5 µg/ml to about 200 µg/ml, 50 µg/ml to about 200 µg/ml, 59 µg/ml, 118 µg/ml in its pharmaceutical composition, and does not expressly teach the concentration of buffer providing particular PH value, and the ionic strength of the composition.

Carling et al. discloses a pharmaceutical composition comprising formoterol (free base) or formoterol fumarate salt in combination with corticosteroid anti-inflammatory

agent, budesonide, in a pharmaceutically acceptable fluid such as a liquid (see col.4 line 2), by inhalation from a nebulizer (see col.3 line 51) for the treatment of respiratory disorders such as asthma (see title and abstract, col.1 lines 10-15, 46-67). Carling et al. also discloses the effective amount of formoterol, 6-100 μg , preferred 6-48 μg (the instant claimed amount within the range of Carling et al.), in a pharmaceutical composition therein (see col.3 lines 44-45). Carling et al. also discloses that a pharmaceutical composition of the combination therein is formulated into a single dosage administration (see Example 1-3 at col.4). Carling et al. also discloses a kit or an article of manufacture comprising the same combination and a nebulizer (see col.3 line 8-10 and 50-52, claims 1-36). Carling et al. also discloses the employment of a tonicity adjusting agent herein such as salts of inorganic or organic salts, e.g., succinate, lactate (see col.3 lines 30-38) and adding oleic acid may improve the physical stability (see col.4 line 12-14).

PDR teaches fluticasone propionate as a known corticosteroid readily employed in the method of treating asthma.

From the teaching of PDR, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ fluticasone propionate in the composition of Hochrainer et al. It is prima facie obvious to combine two agents which are known to be useful to treat asthma individually into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069. The optimization of a result effective parameter, e.g., the effective amounts of active ingredients and excipients in a therapeutic dosage form, is considered within the skill

of the artisan. See, *In re Boesch and Slanev* (CCPA) 204 USPQ 215. The skilled artisan would see a container as a vial useful for multiple uses, absent information the contrary.

It would have been obvious to a person of ordinary skill in the art at the time of invention to optimize parameters such as the concentration of formoterol in its pharmaceutical composition, and the concentration of buffer providing particular PH value, and the ionic strength of the composition. The optimization of a result effective parameter, e.g., the effective amounts of active ingredients and excipients in a therapeutical dosage form, is considered within the skill of the artisan. See, *In re Boesch and Slanev* (CCPA) 204 USPQ 215.

With regard to the limitations "whereby the composition has an estimated shelf-life of greater than 1 month usage time at 25 °C and greater than or equal to 1 year storage time at 5 °C, "whereby greater than 90 % of the initial amount of formoterol in the composition remains at such time", and "the composition is formulated for direct administration", Hochrainer et al. disclose a formulation containing a solvent mixture of ethanol/water, formoterol in a concentration of about 0.9 to about 1.5 mg/ml adjusted to a pH of about 4.5 to about 5.5, and further teaches that the pharmaceutical preparation suitable for administration is obtained by diluting the active substance concentrate with with polar solvents such as water, aqueous saline and adjusting the PH to obtain a stable formulation. See column 8, claim 22. The compositions therein can contain steroids. Thus, absent showing unexpected, and significant benefit residing in the particular limitations herein, the claimed invention would have been obvious to one of skill in the art. Hochrainer et al. particularly teach that the concentrated solution may be

used for making pharmaceutical composition which is such that it can be administered by inhalation using a suitable nebuliser, see col. 4, lines 19-20 and col. 5, lines 33-41. Therefore, it would have been obvious to make a diluted formoterol solution suitable for direct administration. It is noted that fluticasone is not water soluble, therefore, a suspension of fluticasone would have been obvious to one of ordinary skill in the art.

Claim 93 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hochrainer et al. (US 6150418, PTO-892 of record) in view of Carling et al. (US 5674860, PTO-892 of record), and PDR, and further in view of PDR at pages 482, 535, 537, 2828 (of record).

The same disclosures of Hochrainer et al. in view Carling et al. (US 5674860), and PDR have been discussed in the 103(a) rejection set forth above.

Hochrainer et al., Carling et al. do not expressly disclose further adding one or more agent recited in claim 93 herein to the composition.

PDR teaches that albuterol (beta2-adrenoreceptor agonist), accolate (leukotriene receptor antagonist) and Zylflo (5-lipoxygenase inhibitor) are all known to be effective in treating asthma.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a third active such as those enumerated immediately above in a combination composition along with formoterol and fluticasone.

One of ordinary skill in the art would have been motivated to employ a third active such as those enumerated immediately above in a combination composition

along with formoterol and fluticasone because all three actives are known to be useful in treating asthma. Combining two agents which are known to be useful to treat asthma individually into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

Claims 113-116 and 120-121 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hochrainer et al. (US 6150418, PTO-892 of record) in view of Carling et al. (US 5674860, PTO-892 of record), and PDR, and further in view of Hardman et al. (Goodman Gilman's *The Pharmacological Basis of Therapeutics*, 1996, page 665, of record) or Leckie et al (*Novel Therapy Of COPD*, abstract, Jan 2000, of record).

The same disclosures of Hochrainer et al. in view Carling et al. (US 5674860, and PDR have been discussed in the 103(a) rejection set forth above.

Hochrainer et al., Carling et al. and PDR do not expressly disclose further adding an anticholinergic agent such as ipratropium bromide or tiotropium bromide to the composition therein.

Hardman et al. teaches that ipratropium bromide is an anticholinergic agent useful in treating asthma.

Leckie et al teaches that tiotropium is a known bronchodilator employed in treatment of asthma.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a third active such as ipratropium bromide or tiotropium bromide in a combination composition along with formoterol and fluticasone.

One of ordinary skill in the art would have been motivated to employ a third active such as ipratropium bromide or tiotropium bromide in a combination composition along with formoterol and fluticasone because all three actives are known to be useful in treating asthma. Combining two agents which are known to be useful to treat asthma individually into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

Claims 129-146 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hochrainer et al. (US 6,150,418, PTO-892 of record), in view of Remington's Pharmaceutical Sciences, Seventeenth Edition, 1985, pages 1443, 1451.

Hochrainer et al. discloses propellant-free pharmaceutical composition comprising formoterol or its salt (preferably, formoterol fumarate), a known bronchodilator, particularly stable on storage with concentration 10 –500 mg/ml (see col.1 line 65-67; col.2 line 6-11), in aqueous ethanol (water and ethanol are well known polar and protic solvents, see col.2 lines 24-34), in the form of a solution or suspension for use in inhalers for nasal therapy, see abstract and claims 1-4, 8 in particular. Hochrainer et al. further teaches that the pharmaceutical composition is such that it can be administered by inhalation using a suitable nebuliser, see col.4, lines 19-20 and col. 5, lines 33-41. Hochrainer et al. teaches that the pH range is preferably between 2.0-7.0 and most preferably between 4.5-5.5. The employment of inorganic acids, and organic acids such as phosphoric acids, citric acid, tartaric acid (i.e addition of tartaric acid to formoterol, results in instant formoterol tartrate), fumaric acid etc and the employment of

buffers, e.g. phosphate buffers, in its composition are also taught, see in particular col.3, lines 35-40 and col.4 line 55 to col. 5, line 7; and inorganic salts, sodium chloride, and organic salts such as for example, sodium, potassium or ammonium salts of citric acid (see col.2 lines 56-64) in the composition is also taught. Hochrainer et al. teaches the concentration of formoterol to be between about 75 mg/ml and about 500 mg/ml, which may be used with diluent, and other ingredients for the preparation of therapeutical composition. See in particular claims 1-4. Hochrainer et al. also teaches that additional active ingredients such as steroids, anticholinergics could be incorporated in its composition, see claim 19. It is taught that the pharmaceutical preparation suitable for administration is obtained by diluting the active substance concentrate with a pharmacologically suitable solvent. See column 4, lines 21-25. It is taught that the formulation for administration is obtained by diluting to 0.9 mg/ml of formoterol with the diluents such as water, aqueous saline and the PH is adjusted for stable storage. See column 4, lines 26-29; column 5, lines 1-6. A formulation containing a solvent mixture of ethanol/water, formoterol in a concentration of about 0.9 to about 1.5 mg/ml adjusted to a pH of about 4.5 to about 5.5 is also disclosed. See column 8, claim 22.

Hochrainer et al. also discloses a kit or an article of manufacture comprising the same combination and packaging material which include containers, nebulizers. Preferred nebulizers include inhalers. See column 5, lines 33-50. The compositions therein are employed in the methods of treating obstructive respiratory diseases and asthma, see col. 1, lines 1- 37.

Hochrainer et al. does not explicitly teach the concentration of formoterol such as 5 µg/ml to about 200 µg/ml, in its pharmaceutical composition, and does not expressly teach the concentration of buffer providing particular PH value.

It would have been obvious to a person of ordinary skill in the art at the time of invention to optimize parameters such as the concentration of formoterol in its pharmaceutical composition, and the concentration of buffer providing particular PH value. The optimization of a result effective parameter, e.g., the effective amounts of active ingredients and excipients in a therapeutical dosage form, is considered within the skill of the artisan. See, *In re Boesch and Slanev* (CCPA) 204 USPQ 215. Note, sterility of a pharmaceutical composition is an essential element in the practice of pharmacy, and thus is deemed to be obvious. See *Remington's Pharmaceutical Science*, pages 1443, 1451 attached herein. Also, note that the skilled artisan would see a container as a vial useful for multiple uses, absent information to the contrary.

With regard to the limitations "whereby the composition has an estimated shelf-life of greater than 1 month usage time at 25 °C and greater than or equal to 1 year storage time at 5 °C, "whereby greater than 90 % of the initial amount of formoterol in the composition remains at such time", and "the composition is formulated for direct administration", Hochrainer et al. disclose a formulation containing a solvent mixture of ethanol/water, formoterol in a concentration of about 0.9 to about 1.5 mg/ml adjusted to a pH of about 4.5 to about 5.5, and further teaches that the pharmaceutical preparation suitable for administration is obtained by diluting the active substance concentrate with with polar solvents such as water, aqueous saline and adjusting the PH to obtain a

stable formulation. See column 8, claim 22. The compositions therein can contain steroids. Thus, absent showing unexpected, and significant benefit residing in the particular limitation herein, the claimed invention would have been obvious to one of skill in the art. Hochrainer et al. particularly teach that the concentrated solution may be used for making pharmaceutical composition which is such that it can be administered by inhalation using a suitable nebuliser, see col. 4, lines 19-20 and col. 5, lines 33-41. Therefore, it would have been obvious to make a diluted formoterol solution suitable for direct administration. It is noted that fluticasone is not water soluble, therefore, a suspension of fluticasone would have been obvious to one of ordinary skill in the art.

Response to Arguments

Applicant's remarks have been fully considered, but are not found persuasive.

Applicant's remarks on issued patents have been considered. The examiner maintains that issued U.S. Patent is a property, not a precedent. It is pointed out that the examiner will not make any comment on issued US patent.

Applicant argues that "None of the prior art references teach compositions containing formoterol in a dilute solution and steroid anti-inflammatory agent in suspension, which is not only ready for direct administration, but also having long term storage stability. Additionally, none of the prior art references teach such compositions where the concentration of formoterol is about 5 microg/mL to about 200 microg/mL. Regardless of the reference relied upon by the Examiner, one would have to dilute the prior art compositions in order to arrive at the formoterol concentration claimed herein.

Such compositions are therefore not suitable for direct administration." These arguments have been considered, but not found persuasive. Hochrainer et al. discloses propellant-free aqueous pharmaceutical composition comprising formoterol or its salt (preferably, formeterol fumarate), a known bronchodilator, in the form of a solution or suspension for use in inhalers for nasal therapy. PDR teaches fluticasone propionate as a known corticosteroid readily employed in the method of treating asthma. From the teaching of PDR, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ fluticasone propionate in the composition of Hochrainer et al. It is prima facie obvious to combine two agents which are known to be useful to treat asthma individually into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069. As the combined teachings of the prior art renders the claimed composition obvious, the property of such a claimed composition will also be rendered obvious by the prior art teachings, since the properties, namely the formoterol in solution and steroid in suspension in propellant-free water, are inseparable from its composition. Therefore, if the prior art teaches the composition or renders the composition obvious, then the properties are also taught or rendered obvious by the prior art. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990.) See MPEP 2112.01. It is noted that fluticasone is not water soluble, therefore, a suspension of fluticasone would have been obvious to one of ordinary skill in the art. Further, note that the instant claims 129-146 do not contain a steroidal anti-inflammatory agent. For stable storage and immediate use without dilution, the composition need certain amount of tonicity adjusting agent,

buffer, and a limited pH range, see instant specification, examples. Those limitations do not appear in instant claims.

Further, it is noted the particular concentration recited in Hochrainer is merely "for example", and is not a requirement. It is well-settled that disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). Further, Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233,235 (CCPA 1955).

Applicant argues that "The 10 mg/ml lower limit of Hochrainer's range is still 20,000 times higher than the lower limit claimed in the present application. A concentration of 20,000 times higher is not ready to use and Hochrainer specifically discloses diluting the same before use. In contrast, the long term storage suitable pharmaceutical compositions claimed herein are also at the same time, without dilution, suitable for direct administration. In fact, the claims expressly recite this novel aspect of the invention." These arguments have been considered, but not found persuasive. Hochrainer teaches a formulation containing a solvent mixture of ethanol/water, a preservative, Na-EDTA, and dissolved formoterol in a concentration of about 0.9 to about 1.5 mg/ml adjusted to a pH of about 4.5 to about 5.5 is also disclosed. See

column 8, claim 22. Hochrainer further teaches that the pharmaceutical preparation suitable for administration is obtained by diluting the active substance concentrate with with polar solvents such as water, aqueous saline and adjusting the PH to obtain a stable formulation. See column 8, claim 22. The compositions therein can contain steroids. Thus, absent showing unexpected, and significant benefit residing in the particular limitation herein, the claimed invention would have been obvious to one of skill in the art. Hochrainer et al. particularly teach that the concentrated solution may be used for making pharmaceutical composition which is such that it can be administered by inhalation using a suitable nebuliser, see col. 4, lines 19-20 and col. 5, lines 33-41. Therefore, it would have been obvious to make a diluted formoterol solution suitable for direct administration.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The cited references as a whole fairly suggest the employment of the combination of formoterol and steroid compound for treatment of bronchoconstrictive disorders. For example, Hochrainer et al. (6,150,418) teaches that additional active ingredients such as steroids could be incorporated in its composition, see claim 19. It finally teaches that its composition can be employed in methods of treating obstructive respiratory diseases and asthma, see col. 1, lines 1-37.

Applicants contend that Hochrainer reference teaches away from the claimed compositions of the present application where the formoterol is in solution. This argument is not persuasive as it is well settled that disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). Further, a formulation containing a solvent mixture of ethanol/water, dissolved formoterol in a concentration of about 0.9 to about 1.5 mg/ml adjusted to a pH of about 4.5 to about 5.5 is disclosed by Hochrainer. See column 8, claim 22.

Applicants remarks that the claimed compositions have advantages such as direct administration without dilution and/or pH adjusting step which are not obvious over the prior art have been fully considered, but are not persuasive as such benefits is not commensurate in scope with the claimed invention. For stable storage and immediate use without dilute, the composition need certain amount of tonicity adjusting agent, buffer, and a limited pH range, see the examples. Those limitations do not appear in instant claims.

Applicant argues that "The shortcomings of Hochrainer are not cured by the secondary reference. The Examiner cited Carling as disclosing a formoterol concentration of 6-100 microg (col. 3, line 44). However, this is a dry powder concentration of formoterol, not formoterol in solution as claimed in the present application." These arguments have been considered, but not found persuasive. Carling et al. reference was employed for its teaching that a formoterol (free base) or formoterol fumarate salt is used in combination with corticosteroid anti-inflammatory agent,

budesonide, for the treatment of respiratory disorders such as asthma (see title and abstract, col.1 lines 10-15, 46-67). Carling et al. also discloses the effective amount of formoterol, 6-100 μg , preferred 6-48 μg , the instant claimed amount is within the range of Carling et al. i.e Carling et al. teaches the effective amount that can be used to treat respiratory disorders such as asthma. Accordingly, there is clear motivation to employ formoterol in an amount of 6-100 μg in combination with another corticosteroid anti-inflammatory agent, fluticasone as discussed above.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period, will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Friday, 8am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shobha Kantamneni, Ph.D
Patent Examiner
Art Unit 1617

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617

Search Notes (continued)

Application/Control No.

09/887,496

Applicant(s)/Patent under
Reexamination

BANERJEE ET AL.

Examiner

Shobha Kantamneni

Art Unit

1617

SEARCHED

Class	Subclass	Date	Examiner
514	727	7/7/2009	KS
514	730,734	7/7/2009	KS
514	169	7/7/2009	KS
514	170,177	7/7/2009	KS
514	178,182	7/7/2009	KS

INTERFERENCE SEARCHED

Class	Subclass	Date	Examiner

**SEARCH NOTES
(INCLUDING SEARCH STRATEGY)**

	DATE	EXMR
Inventor search updated	7/7/2009	KS
Search updated	7/7/2009	KS